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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/426,792	10/22/1999	DENNIS T. MANGANO	9114-004-999	2354

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	23

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary

Application No.	Applicant(s)
09/426,792	Mangano
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 13, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-16, 49-51, and 53-55* is/are pending in the application.

4a) Of the above, claim(s) *7-12* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6, 13-16, 49-51, and 53-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's Response filed January 13, 2003, Paper No. 21, is acknowledged. Claims 1-16, 49-51 and 53-55 remain under consideration. Claims 7-12 remain withdrawn from consideration as being directed to non-elected inventions, 37 C FR 1.142(b). Claims 1-6, 13-16, 49-51 and 53-55, directed to β1-adrenergic blockers, remain under consideration.

In the last Office Action claims 1-6, 13-16 and 49-55 were rejected under 35 U.S.C. 103(a) as being unpatentable over Goldstein et al., J. Cardiovasc. Pharmacology., particularly in view of Kataria et al., J. Cardiothoracic Anest.

It was asserted Goldstein teaches the administration of a therapeutic dose of the β1-selective blocking agent atenolol to patients immediately following cardiac-related surgery. Atenolol decreased both heart rate and blood pressure. No patient with bronchospasm, bradycardia, atrioventricular conduction defects, heart failure or recent myocardial infarction was included. See lines 4-10, column 2, page 254. As required by claims 15 and 16, patients suffering from coronary artery disease and those at risk for coronary artery disease were included. Although Goldstein's patient population all underwent coronary artery bypass, the parameters following atenolol administration are also monitored in non-cardiac related surgery.

Applicant argues Goldstein does not teach treatment prior to or during surgery and that the assertion that administration of atenolol immediately following cardiac surgery is incorrect. Applicant urges treatment with atenolol was started two hours after extubation and administration *could occur* as late as 14 to 20 hours after surgery.

Further, Applicant argues there was an interruption of treatment with the beta-blocker 24 hours before surgery.

Applicant's arguments have been given careful consideration but are not found persuasive. The rejection of record is repeated for the reasons of record. There is no support on the record that patients undergoing bypass surgery were not extubated until "up to 12-18 hours after surgery" in 1993. Further, the present claims are not limited to bypass surgery. Rather, the recitation "surgery" in claims 1, 49 and 53 encompasses any surgical procedure. The secondary reference, Kataria, teaches the administration of the β_1-adrenergic clocking agent, esmolol, intraoperatively and immediately after general surgery, during emergence from anesthesia, to reduce cardiovascular disease complications as tachycardia and/or hypertension. See the second paragraph of column one under the abstract on page 13. It is noted that administration of the beta-blocker before surgery is not a requirement of any of the claims.

One skilled in the cardiology art would have been motivated to administer a β_1-selective blocking agent to reduce cardiovascular complications following surgery in view of the combined teachings of Goldstein and Kataria wherein every limitation of claims 1, 49 and 53 is taught or suggested. Doses ranging from 100 to 2,104 mg of esmolol would reasonably meet the limitation in claims 1, 49 and 53 "near the maximum effective dose". A heart rate at or slightly above 65 bpm and a systolic blood pressure reading slightly over 100 Hg mm would have reasonably been considered desirable and within the normal range. The selections of both an optimal heart rate and systolic pressure are parameters well within the purview of the skilled cardiologist through no

more than routine experimentation. It would have been reasonable to expect no patient would have been discharged from a hospital with congestive heart failure, third degree heart block or bronchospasm. Esmolol and atenolol are well established in the prior art as effective agents for reducing cardiovascular complications, as decreasing heart rate and blood pressure, following surgery. The continued administration of the β_1-adrenergic agent following surgery is conventional.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C FR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C FR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

April 18, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER